MAIL BOX AFTER FINAL RESPONSE
Attorney Docket 26775U

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Appl. of:	Naphtali Savion	: Examiner:	Zhoreh Fay
Serial No.	09/341,048	: Group Art Unit:	1618
Filed:	August 9, 1999		

For: **TREATMENT OF THE EYE WITH A PHARMACEUTICAL COMPOSITION**

DECLARATION UNDER 37 C.F.R. 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir/Madam:

The undersigned, Emidio Fedeli, hereby declare and say as follows.

1. I am a citizen of Italy, residing at Ciampino (Rome).
2. I have been awarded the degree of Doctor in Chemistry by the University of Rome.
3. I am currently, and have been for 8 years the Director for Research and Development Tubilux Pharma SpA, in Pomezia, Italy.
4. I am fully conversant with the medical conditions and pharmaceutical compositions employed for that purposes included in the subject matter of U.S. Patent Application Serial No. 10/048,789.
5. The following clinical study was conducted under my supervision.

6. Clinical Study

6.1 The composition employed for this study, TBX-024, contained the following ingredients in the following amounts:

Soya oil	1.25 % (w/v)
Mean chain triglycerides (MCT)	1.25 % (w/v)
Egg phospholipids	0.30 % (w/v)
Glycerol	2.15 % (w/v)
Methyl-p-hydroxybenzoate	0.05 % (w/v)
Propyl-p-hydroxybenzoate	0.01 % (w/v)
Tocopherol	0.02 % (w/v)
Purified water	q.s. to 100ml

6.2 The primary objective of this pilot study was to evaluate the effect of a phospholipid-based microemulsion named TBX-024, which is the subject of U.S. Patent Application No. 09/341,048, on both the extent of the erosion and the recovery time.

6.3 The secondary objective was to evaluate the effect of TBX-024 on either the objective or subjective symptoms and on ocular and systemic tolerance.

7. Study Design

The study was designed as a randomized single blind clinical study, and conducted as follows:

7.1 Thirty patients suffering from non-infectious corneal erosion were included in the study.

7.2 Fifteen patients were then treated each with one drop, four times a day for five days of TBX-024 having the composition described above.

7.3 The remaining 15 patients were treated with 0.2% sodium hyaluronate (HA), which was instilled with one drop, four times a day for five days.

8. Evaluation Criteria/Efficacy Variables

For evaluation of the study, certain criteria were developed.

8.1 A primary efficacy variable was developed to measure the size of the lesion by fluorescein staining and for the complete recovery time in hours.

8.2 A secondary efficacy variable used Visual Analogic Scales (VAS) for subjective and objective symptoms.

8.3 A subjective symptom was classified either as feelings of pain, lachrymation, photophobia or foreign body sensation.

8.4 An objective symptom was classified as conjunctival hyperemia, chemosis or edema.

8.5 The last criterion used was tolerability, with a global local tolerance assessment by an investigator on a VAS and a global local tolerance assessment by the patient on a VAS. These assessments were used to asses systemic safety variables and to evaluate adverse events.

9. Results

9.1 Efficacy

The results of this study demonstrated that the patients treated with the TBX-024 had a faster recovery time and a faster reduction of the severity of both the possible objective and the subjective symptoms

when compared to the patients that received the HA treatment. Both products employed in the study were judged efficacious by an investigator and the patients.

9.2 Tolerability & Safety

With regards to tolerability and safety, both local and systemic tolerance appeared to be very good with both of the study products.

10. Conclusion

The results of this pilot study showed a trend towards better efficacy for the treatment with TBX-024, the treatment of the above-identified patent application, than for the treatment with HA. The treatment of the above-identified patent application performed better, although not yet statistically significantly, in terms of accelerating the patient's recovery time and of reducing the severity of symptomatology. Further studies are in progress to demonstrate the clinical efficacy of TBX-024 in wound healing.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with knowledge that willful false statements and the like are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that willful false statements may jeopardize the validity of the application or any patent issuing thereon.

September 6, 2005

Date

Dr. Emidio Fedeli
Research and Development Director
Tubilux Pharma SpA